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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/823,712

03/30/2001

Gregor Sagner

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ROCHE MOLECULAR SYSTEMS INC
PATENT LAW DEPARTMENT
1145 ATLANTIC AVENUE
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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/823,712

Applicant(s)

SAGNER ET AL.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-17,23-26 and 31-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-17,23-26 and 31-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on March 31, 2004, has been entered.
2. Claims 15-17, 23-26, 31-39 are pending Claims 1-14, 18-22, 27-30 are cancelled.
3. This application is filed on March 30, 2001.

Response to Arguments

4. Applicant's response to the office action is fully considered and is found persuasive.
5. With regard to the rejection made in the previous office action under 35 USC 103(a), Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein in view of the amendment and new grounds of rejections.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 16 and 17 are unclear and indefinite for being dependent on cancelled claims 11 and 14.

B. Claim 17 recites the limitation "said DNA-binding dye". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 15-16, 23-26, 31-35, 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al. (WO 99/54510) in view of Meijerink et al. (J Mol. Diagnostics, Vol. 3, No. 2, 2001).

Lowe et al. teach a method for determining a quantitative measure of an amplification of a target nucleic acid of claims 15-16, 23-26, 31-33, 38-39 comprising the steps of

(a) preparing a dilution series of the target nucleic acid (see page 3, line 12-14, page 6, line 20-28, page 11, line 24-35);

(b) amplifying the target nucleic acid under defined conditions and measuring the amplification in real-time (see page 3, line 14-25);

(c, d) setting a defined signal threshold value and determining for each dilution, the cycle number at which the signal threshold value is exceeded (threshold cycle for each dilution) (see page 3, line 25-27, page 10, line 16-23);

(f) calculating the amplification equivalent in each dilution series and normalizing the RNA equivalent to provide normalized RNA equivalent standard curve. (see page 3, line 29-33, page 10, lines 31-39).

With regard to claim 23, 25, Lowe et al. teach determining concentration of the target nucleic acid (see page 12, line 9-15);

With regard to claim 31-33, Lowe et al. teach quantifying the amount of target nucleic acid relative to the reference nucleic acid (see page 13, line 30-39, page 14, line 1-19);

With regard to claims 38- 39, Lowe et al teach a method for quantitating a target nucleic acid using internal standard or reference nucleic acid (see page 13, line 10-39);

With regard to claims 34-35, Lowe et al. teach said amplified nucleic acid is detected using fluorescently labeled probe such as TAQMAN probes or FRET probes (see page 10, line 1-30, page 8, line 29-36).

However, Lowe et al. did not teach determining the efficiency of an amplification by determining a non-linear continuously differentiable function of a logarithm of copy number.

Meijerink et al. teach a method for determining amplification efficiencies for different DNA samples by real-time PCR, wherein Meijerink et al. teach that the method comprises calculating the amplification reaction efficiency and normalizing to a reference value using dilution series related to the logarithm of dilution factor or efficiency compensation control using

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a polynomial equation as a measure of reaction efficiency (see page 56, column 1, paragraphs 1-3, column 2, paragraphs 1-3, page 57, col. 1, paragraphs 4-5).

Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of determining quantitative measure of an amplification of a target nucleic acid as taught by Lowe et al. with the step of calculating the amplification efficiency in relation to a reference as taught by Meijerink et al. to achieve expected advantage of developing an improved sensitive method for determining the efficiency of an amplification of a target nucleic acid because Meijerink et al. taught that differences in amplification efficiencies in different samples result in the underestimation of a quantitative measure or false negative result of a target DNA in quantitative PCR analysis. Calculation of the exact efficiencies based on threshold cycle values and calibration of the samples with a reference would result in an accurate estimate of the target DNA, regardless of the quality of the DNA (see page 56, paragraph 1). An ordinary practitioner would have been motivated to combine the method of determining a quantitative measure of a target nucleic acid as taught by Lowe et al. with the inclusion of the step of determining the efficiency of an amplification to enhance the sensitivity by reducing background noise or false negatives in the quantitation of said target nucleic acid in a sample.

B. Claims 17, 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al. (WO 99/54510) in view of Meijerink et al. (J Mol. Diagnostics, Vol. 3, No. 2, 2001) as applied to claims 15-16, 23-26, 31-35, 38-39 above, and further in view of Wittwer et al. (USPN. 6,174,670).

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Lowe et al. in view of Meijerink et al. teach a method for determining the efficiency of an amplification of a target nucleic acid as discussed above in section 7A.

However, Lowe et al. in view of Meijerink et al. did not teach detecting amplified nucleic acid using a DNA- binding dye, SYBR Green I.

Wittwer et al. teach a method for monitoring and quantitating target nucleic acid during PCR, wherein Wittwer et al. disclose that the method utilizes DNA-binding dye, SYBR Green I for monitoring and quantitating target nucleic acid (see col. 7, line 14-31).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a method of determining the efficiency of amplification and quantitating a target nucleic acid as taught by Lowe et al. in view of Meijerink et al. with the step of detecting amplified nucleic acid using SYBR Green I dye as taught by Wittwer et al. to achieve expected advantage of developing an improved sensitive method for quantitating a target nucleic acid because Wittwer et al. taught that SYBR Green I is a preferred double-strand-specific dye for fluorescence monitoring of PCR, primarily because of superior sensitivity, arising from greater discrimination between double stranded and single stranded nucleic acid, and is inexpensive dye (see column 23, line 9-16). An ordinary practitioner would have been motivated to combine the method of determining the efficiency of an amplification of a target nucleic acid and quantitation of said nucleic acid as taught by Lowe et al. with the inclusion of the step of detecting amplified nucleic acid using SYBR Green I dye to enhance the sensitivity of quantitation of a target nucleic acid and for cost-effective purposes.

Conclusion

No claims are allowable.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

^{SC}
Suryaprabha Chunduru
August 2, 2004


JEFFREY FREDMAN
PRIMARY EXAMINER
8/5/04